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SCIENTIFIC OPINION

Safety and efficacy of a feed additive consisting of inactivated selenised yeast (*Saccharomyces cerevisiae* CCTCC M 2022402) for all animal species (Phytobiotics Futterzusatzstoffe GmbH)

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Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the safety and efficacy of the selenised yeast (inactivated) *Saccharomyces cerevisiae* CCTCC M 2022402 (Plexomin® Se 3000, available in two forms: 'granules' and 'micro') as a nutritional feed additive for all animal species. Based on a tolerance–efficacy trial, the FEEDAP Panel concluded that the additive is safe for chickens for fattening at proposed conditions of use and this conclusion can be extrapolated to all animal species. In the absence of deposition data in all animal species and products, the FEEDAP Panel cannot conclude on the safety for the consumer. Plexomin® Se 3000 (granules) is dust-free; therefore, the exposure through inhalation is unlikely. Plexomin® Se 3000 (micro) presents a risk by inhalation. Both forms of the additive (granules and micro) are considered as respiratory sensitisers. Due to the lack of data, no conclusions can be drawn on the dermal and eye irritation potential of Plexomin® Se 3000 (granules). Plexomin® Se 3000 (micro) is not irritant to the skin and the eyes. No conclusions can be drawn on the potential of both forms of the additive to be dermal sensitisers. The use of the additive in animal nutrition is considered safe for the environment. The additive is an efficacious source of selenium in feedingstuffs for all animal species.

KEYWORDS

compounds of trace elements, efficacy, feed additive, nutritional additives, Plexomin® Se 3000, *Saccharomyces cerevisiae* CCTCC M 2022402, safety, selenised yeast

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1 | INTRODUCTION

1.1 | Background and Terms of Reference

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of feed additive shall submit an application in accordance with Article 7.

The European Commission received a request from Phytobiotics Futterzusatzstoffe GmbH[2] for the authorisation of the additive consisting of inactivated selenised yeast *Saccharomyces cerevisiae* CCTCC M 2022402, when used as a feed additive for all animal species (category: nutritional additives; functional group: compounds of trace elements).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 4(1) (authorisation of a feed additive or new use of a feed additive). The dossier was received on 22 March 2021 and the general information and supporting documentation are available at https://open.efsa.europa.eu/questions/EFSA-Q-2021-00309. The particulars and documents in support of the application were considered valid by EFSA as of 20 October 2021.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of the feed additive consisting of selenised yeast produced by *S. cerevisiae* CCTCC M 2022402 inactivated, when used under the proposed conditions of use (see **Section 3.1.6**).

1.2 | Additional information

The additive is an inactivated selenised yeast produced with *Saccharomyces cerevisiae* CCTCC M 2022402 intended to supply organic selenium in animal nutrition. This additive has not been previously authorised as a feed additive in the European Union.

The FEEDAP Panel previously assessed safety and efficacy of selenium-enriched yeasts (EFSA FEEDAP Panel, 2009a, 2012a, 2016, 2017, 2018a, 2019a, 2020, 2021).

There are several inactivated selenised yeasts authorised in the EU produced by different strains of *S. cerevisiae* (CNCM I-3060 (3b810 and 3b810i),[3] NCYC R397 (3b811),[4] CNCM I-3399 (3b812),[5] NCYC R646 (3b813)[6] and NCYC R645 (3b817)[7]).

Currently, the maximum authorised supplementation with organic selenium is 0.2 mg Se/kg of complete feed (with a moisture content of 12%), while the maximum total selenium is 0.5 mg/kg complete feed.

2 | DATA AND METHODOLOGIES

2.1 | Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier[8] in support of the authorisation request for the use of inactivated selenised yeast produced with *S. cerevisiae* CCTCC M 2022402 (Plexomin® Se 3000/Plexomin® Se 3000 micro) as a feed additive.

The confidential version of the technical dossier was subject to a target consultation of the interested Member States from 20 October 2021 to 20 January 2022 for which the received comments were considered for the assessment.

[1]Regulation (EC) No 1831/2003 of the European Parliament and of the council of 22 September 2003 on the additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.

[2]Phytobiotics Futterzusatzstoffe GmbH, Vallufer Strasse 10a, 65,343 Eltville, Germany.

[3]Commission Implementing Regulation (EU) 2019/804 of 17 May 2019 concerning the renewal of the authorisation of organic form of selenium produced by *Saccharomyces cerevisiae* CNCM I-3060 and of selenomethionine produced by *Saccharomyces cerevisiae* NCYC R397 as feed additives for all animal species and repealing Regulations (EC) No 1750/2006 and (EC) No 634/2007.

[4]Commission Implementing Regulation (EU) 2019/804 of 17 May 2019 concerning the renewal of the authorisation of organic form of selenium produced by *Saccharomyces cerevisiae* CNCM I-3060 and of selenomethionine produced *by Saccharomyces cerevisiae* NCYC R397 as feed additives for all animal species and repealing Regulations (EC) No 1750/2006 and (EC) No 634/2007.

[5]Commission Implementing Regulation (EU) 2020/2117 of 16 December 2020 concerning the renewal of the authorisation of selenomethionine produced by *Saccharomyces cerevisiae* CNCM I-3399 with the new name 'selenised yeast *Saccharomyces cerevisiae* CNCM I-3399' as a feed additive for all animal species, and repealing Regulation (EC) No 900/2009.

[6]Commission Implementing Regulation (EU) No 427/2013 of 8 May 2013 concerning the authorisation of selenomethionine produced by *Saccharomyces cerevisiae* NCYC R646 as a feed additive for all animal species and amending Regulations (EC) No 1750/2006, (EC) No 634/2007 and (EC) No 900/2009 as regards the maximum supplementation with selenised yeast.

[7]Commission Implementing Regulation (EU) No 2015/489 of 23 March 2015 concerning the authorisation of selenomethionine produced by *Saccharomyces cerevisiae* NCYC R645 as a feed additive for all animal species.

[8]Dossier reference: FAD-2021-0045.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA or other expert bodies, peer-reviewed scientific papers, other scientific reports and experts' knowledge, to deliver the present output.

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of the selenomethionine and total selenium in the feed additive and total selenium in premixtures and feedingstuffs.[9]

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of the active substance (trade name of the product) is in line with the principles laid down in Regulation (EC) No 429/2008[10] and the relevant guidance documents: Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012b), Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017b), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEEDAP Panel, 2017c), Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017d), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018b), Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018c) and Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019b).

3 | ASSESSMENT

The additive under assessment contains inactivated selenised yeast *Saccharomyces cerevisiae* CCTCC M 2022402 and is intended to be used as a nutritional additive (functional group: trace elements) in feed for all animal species.

3.1 | Characterisation

3.1.1 | Characterisation of *Saccharomyces cerevisiae* CCTCC M 2022402

The additive is produced by the use of a non-genetically modified strain of *Saccharomyces cerevisiae* deposited in the China Center for Type Culture Collection (CCTCC) with the accession number CCTCC M 2022402.[11] [redacted]

Taxonomic identification of the strain as *S. cerevisiae* was evaluated by whole genome sequencing (WGS)-based analyses.[12] Two approaches were used, alignment-free genome distance estimation and multigene phylogenetics analysis ([redacted] The alignment-free genome distance estimation analysis supported the reference genome *S. cerevisiae* S288C as the closest genome and the multigene phylogenetic analysis showed that the strain CCTCC M 2022402 clustered with other *S. cerevisiae* strains. Therefore, the identity of the strain CCTCC M 2022402 as *S. cerevisiae* was confirmed. No plasmids were detected by gel electrophoresis.[13]

3.1.2 | Manufacturing process

The manufacturing process is fully described in the technical dossier.[14] [redacted][15] [redacted][16] The additive is available in two forms, Plexomin® Se 3000 (granules) and Plexomin® Se 3000 (micro). [redacted]

[9]The full report is available on the EURL website: https://joint-research-centre.ec.europa.eu/publications/fad-2021-0045-0_en

[10]Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.

[11]Technical dossier/Supplementary Information January 2023/Annex_SIn_13.

[12]Technical dossier/Section II/Annex II.82.

[13]Technical dossier/Section II/Annex II.82.

[14]Technical dossier/Section II Identity.

[15]Technical dossier/Section II/Annex II.103.

[16]Technical dossier/Section II/Annex II.93.

[redacted][17] [redacted]
[redacted][18,19] [redacted]

The applicant states that no antimicrobials are used in the manufacturing process.[20]

3.1.3 | Characterisation of the additive

The additive is produced in two forms, Plexomin® Se 3000 (granules) and Plexomin® Se 3000 (micro). [redacted] The additive (both forms) is specified[21] to contain (on as is basis) a minimum of 3000 Se mg/kg additive, with a minimum of 98% organic selenium, and a minimum of 63% of total selenium in the form of selenomethionine (Se-Met).

The additive is also specified to contain a minimum of 40% crude protein,[22] maximum 8% of crude ash and a maximum of 8% moisture.

Proximate analyses were provided for three batches[23] of the additive (form not specified): dry matter was on average [redacted], crude protein [redacted] crude ash [redacted] fat [redacted] and fibre [redacted] It is noted that approx. 46% of the additive could not be analytically identified and it is assumed to be mainly composed of the yeast biomass.

Analytical data to confirm the specification in terms of selenium contents were provided for both forms of the additive (granules and micro).

Free unbound selenate and selenite were not detected (threshold of [redacted]) in any sample (granulated and micro).[24]

Plexomin® Se 3000 (granules)

Nine batches of Plexomin® Se 3000 granules were analysed[25] and showed an average content of total selenium of [redacted]; the average content of selenium from Se-Met was [redacted] corresponding to an average fraction of selenium from Se-Met of [redacted] the content of selenium from [redacted] was analysed in nine batches and was on average [redacted], corresponding to an average of [redacted] It is noted that four out of nine batches did not comply with the specification of minimum of 3000 mg total Se/kg additive; and four out of nine batches did not comply with the specified minimum of 63% selenium from Se-Met.

The FEEDAP Panel notes that these deviations with respect to the minimum selenium content may be within the limits of the accuracy of the analytical method, with the exception of two batches out of nine, which did not comply with the minimum specified selenium content from Se-Met (min 63%), even after considering the reported analytical measurement error.

It is noted that only about 75% of compounds containing selenium in the additive is identified (Se-Met [redacted]). In order to provide more details on the unidentified organic fraction (about 25%) containing selenium, the applicant submitted the analytically determined[26] content [redacted][27] [redacted]

Cadmium, lead and arsenic[28] levels in three batches of the granulated form of the additive were below the limit of quantification (LOQ),[29] whereas mercury [redacted]. Polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), dioxin-like polychlorinated biphenyls (DL-PCBs) and non-DL-PCBs were analysed in three batches of the additive. [redacted][30] [redacted][31].

[17] Technical dossier/Section II/Annex II.112.
[18] [redacted] is currently under re-evaluation.
[19] Technical dossier/Supplementary information 2024-01-22/ Annex Sin IV_2 and Annex Sin IV_3.
[20] Technical dossier/Section II/Annex II.64.
[21] Technical dossier/Section II/Annex II 1 and 2 and Section II Identity.
[22] Protein nitrogen (N) determination using the Dumas method.
[23] Technical dossier/Section II/Annex II.59.
[24] Technical dossier/Section II/Annex II.58; Supplementary information 2023-02-27/Annexes Sin 2, 3, 4 and 5.
[25] Technical dossier/Section II/Annex II.58 and Supplementary information 2023-02-27/Annex SIn 4 and SIn 5.
[26] Technical dossier/Section II/Supplementary information 2023-02-27/Annex Sin_4 and 5.
[redacted]
[28] Technical dossier/Section II/Annex II.63.
[redacted]
[31] Technical dossier/Section II/Annex II 63. [redacted]

Microbiological contamination was analysed in three batches.[32]

Eight samples from three independent batches[33] of Plexomin® Se 3000 (granules) were analysed for viable yeast cells by plating serial dilutions on Rose Bengal Chloramphenicol agar. No growth was detected with a method reaching a limit of detection (LOD) of < 100 CFU/g.

Plexomin® Se 3000 (micro)

To confirm the specification, analysis of five batches of the micro form of the additive were provided.[34] Total selenium content was on average . Selenium content from Se-Met was on average corresponding to average content of selenium from corresponding to of total organic selenium.

In order to provide more details on the unidentified organic fraction (about 25%) containing selenium, [35]

Cadmium, lead, mercury and arsenic were all below the limit of detection.[36] The analysis of mycotoxins showed values below the respective LOQs.[37]

Microbiological contamination was analysed in three batches.[38]

Eight samples from three independent batches of Plexomin Se 3000 (micro) were analysed for viable yeast cells . No growth was detected with a method reaching an LOD of < 100 CFU/g.[39]

The FEEDAP Panel considers that the microbial contamination and the amounts of the detected impurities do not raise safety concerns.

3.1.4 | Physical properties of the additive

Plexomin® Se 3000 (granules) is a beige, dust-free granulate with a bulk density[40] of 580 kg/m^3, whereas Plexomin® Se 3000 (micro) is a beige powder with bulk density[41] of 400 kg/m^3.

The dusting potential of three batches (four replicates each) of both forms of the additive was determined using the Stauber-Heubach method.[42,43]

The particle size distribution of three batches of each form of the additive [44] [45]

Selenium content and particle-size distribution were tested in three batches [46]

[32]Technical dossier/Section II/Annex II.63.
[33]Technical dossier/Section II/Annex II.95 and Annex II.96.
[34]Technical dossier/Supplementary information 2023-02-27/Annex Sin_2 and Annex Sin_3.
[36]Technical dossier/Supplementary information 2023-2-27/ Annex SIn 6 and 7;
[38]Technical dossier/Supplementary information 2023-02-27/Annex Sin_6.
[39]Technical dossier/Section II/Annex II.98.
[40]Technical dossier/Section II/Annex II.1.
[41]Technical dossier/Section II/Annex II.2.
[42]Technical dosser/Section II/Annex II.65.
[43]Technical dossier/Section II/Annex II.67.
[44]Technical dossier/Section II/Annex II.66.
[45]Technical dossier/Section II/Annex II.68.
[46]Technical dossier/Section II/Annex II.69 and Annex II.70.

[redacted][47]

The Panel notes that Se-Met [redacted] soluble in water[48] above the threshold considered by the Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles (EFSA Scientific Committee, 2021). Proteins and biomass are expected to undergo the same digestion and metabolic pathways as other components of feed.

3.1.5 | Stability and homogeneity

For compounds of trace elements, stability studies are generally not required. The shelf-life of the additive was tested in three batches of both forms of the additive (granules and micro) when stored in commercial packaging at 25°C/65% relative humidity (RH) for 24 months.[49] At the end of the storage period, the loss of total selenium was [redacted] and [redacted] (micro). The granulated form of the additive (three batches) was also stored at 40°C/75% RH for 12 months, and the loss of total selenium at the end of the study was up to [redacted].[50]

The capacity for homogeneous distribution of each form of the additive in a complementary feed for dairy cows (based on rapeseed meal, palm-expeller, grit of sugar beets, maize, wheat bran) was studied in 10 subsamples when supplemented at the intended level of [redacted] complementary feed. Total selenium was analysed and the coefficient of variation (CV) was [redacted] (granular form)[51] and [redacted] (micro form).[52]

3.1.6 | Conditions of use

The additive is intended for use in feed for all animal species. It should be incorporated to compound feed via premixtures. No minimum concentration nor withdrawal period is proposed. The proposed maximum concentration in compound feed is:

- 0.2 mg organic Se/kg
- 0.5 mg total Se/kg.

These provisions are in line with the current authorisations for different sources of selenium as a feed additive (see Section 1.2).

3.2 | Safety

3.2.1 | Safety of *S. cerevisiae* CCTCC M 2022402

S. cerevisiae is considered by EFSA to be suitable for the qualified presumption of safety (QPS) approach to safety assessment (EFSA BIOHAZ Panel, 2024). The identity of the strain CCTCC M 2022402 as *S. cerevisiae* was confirmed. Consequently, *S. cerevisiae* CCTCC M 2022402 can be presumed safe for the target species, the consumer and the environment.

3.2.2 | Safety for the target species

The applicant submitted one tolerance trial in chickens for fattening[53] to support the safety of the additive for the target species. [redacted][54] The content of selenium in the feeds was confirmed analytically (see Table 1). The experimental diets were offered ad libitum for 37 days.

[47]Technical dossier/Section II/Annex II.71 and Annex II.72.

[48]The solubility of SeMet is reported to be 50 g/L https://www.chemspider.com/Chemical-Structure.94765.html. [redacted]

[49]Technical dossier/Supplementary information 2023-02-27/Annex Sin_9 and 10.

[50]Technical dossier/Section II/Annex II.113.

[51]Technical dossier/Section II/Annex II.114.

[52]Technical dossier/Section II/Annex II.115.

[53]Technical dossier/Supplementary information 2023-02-27/Annex Sin_16 and Supplementary information 2023-06-06/Annex Sin II_3.

[54]Technical dossier/Supplementary information 2024-01-22/Annex_SIn_IV_4 and Supplementary information 2023-02-27/Annex Sin 16.

TABLE 1 Se content in the experimental diets offered to the different experimental groups.

Source of selenium	Intended organic Se supplementation (mg/kg complete feed)	Total* Se (mg/kg complete feed)	
		Starter	Grower
None	–[1]		
Plexomin® Se 3000			
Plexomin® Se 3000			
Other selenised yeast			

*

[1]No selenium added.

Mortality and general health status were monitored throughout the study. Dead animals were necropsied, and the most likely cause of death or reason for culling recorded. The pen body weight was recorded at the beginning of the experiment (day 1). Thereafter, pen body weight and feed intake were recorded on days . The average daily gain, average daily feed intake and the feed to gain ratio were calculated and corrected for mortality for the overall period. At the end of the study (day 37), two birds per pen were randomly selected, killed, weighted and blood samples collected. Haematology, [55] biochemistry [56] analyses and a gross pathology [57] evaluation was performed in all treatment groups, excluding treatment groups corresponding to supplementation at mg Se/kg feed, . After the gross pathology, the heart, kidneys, liver, spleen and breast muscle were weighed. In the birds from the control and both groups supplemented at mg Se/kg feed, samples of serum, liver, kidneys, breast muscle and abdominal fat were collected (see Section 3.2.3.2).

The data were statistically analysed with a generalised linear model, with the diet and block (location of pen in the house) as fixed effects. Group means were compared with Tukey test. The significance level was established at 0.05.

The average overall mortality rate was , with no differences between treatments (Table 2). The Panel noted a relatively high mortality/culling rate during the starter phase of the trial with the additive under assessment. The applicant provided evidence[58] Therefore, the Panel considers that the trial can support the evaluation of the safety for the target species.

No adverse effects were observed in the performance parameters for any of the supplemented groups with respect to the control. The only effects observed were an improved feed to gain ratio on both overdose groups with respect to the control.

TABLE 2 Performance parameters and mortality in chickens for fattening after 35 days.

Source of selenium	Added Se (mg/kg complete feed)	Total feed intake (g/bird)	Final body weight (g)	Feed-to-gain ratio	Mortality and culling % (*n*)
None	–				
Plexomin® Se 3000					
Plexomin® Se 3000					

[a,b]Mean in a column not sharing a common letter are statistically different ($p < 0.05$).

No differences were observed between the Se-supplemented groups and the control in most of the haematological and biochemistry parameters, except for the content of which was higher in the control , compared to the Plexomin® Se 3000 overdose level . However, this difference was not considered an adverse effect.

[58]Technical dossier/2023-06-06 Supplementary information/Annex Sin II_3.

At supplementation level of [redacted] mg Se/kg feed, there was significantly higher selenium contents in [redacted] of both treatment groups and [redacted] ([redacted]) in the same treatment groups, compared to the same parameters in the control group ([redacted]) (see also Table 4).

No differences between treatments were observed in gross pathology and organ weights.

3.2.2.1 | *Conclusions on safety for the target species*

The additive is safe up to the highest selenium concentration authorised in complete feed (0.2 mg Se/kg feed, from organic source; 0.5 mg total Se/kg feed). This conclusion is extrapolated to all animal species and categories at the same use level.

3.2.3 | Safety for the consumer

The applicant did not provide any new absorption, distribution, metabolism, and excretion (ADME) or toxicological studies with the additive under assessment.[59]

The FEEDAP Panel adopted several opinions on the safety of selenium, in its inorganic forms (EFSA FEEDAP Panel, 2015), and deriving from different *Saccharomyces cerevisiae* strains (EFSA FEEDAP Panel, 2006, 2007, 2009a, 2017a, 2018a, 2019a, 2020, 2021) or other organic selenium sources (EFSA FEEDAP Panel, 2009b, 2013). In these opinions, the Panel evaluated the ADME and toxicology of Se and assessed most of the published studies submitted by the applicants. The FEEDAP Panel assessed the safety for the consumer by comparing the exposure of the consumer with the available health-based guidance value, in particular with the tolerable upper level (UL) for selenium of 300 μg Se/day (for adults) and with the available ULs for children (EFSA FEEDAP, 2006, 2007, 2011). The UL of 300 μg Se/day (for adults) was set by the European Commission Scientific Committee on Food (SCF, 2000) based on the data from the cross-sectional study by Yang et al. (1989).

In 2022, the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) adopted a Scientific opinion on the tolerable upper intake level for selenium (EFSA NDA Panel, 2023). In this recent opinion, the NDA Panel revised all the available information related to the ADME and toxicological properties of selenium and proposed to lower the UL compared to the previous value (300 μg Se/day for adults) and established ULs for different age categories. In its opinion, the NDA Panel used the lowest-observed-adverse-effect level (LOAEL) of 330 μg/day identified from the randomised control trial in men, SELECT (Lippman et al., 2009) as a reference point for the derivation of the UL for selenium. The LOAEL identified was associated with an increased risk of developing alopecia, an early sign of selenium toxicity. EFSA NDA Panel set a new UL for selenium of 255 μg Se/day for adults (including pregnant and lactating women) and extrapolated the UL from adults to infants, children and adolescents based on body weights. The UL values established for the different age categories are 45 μg Se/day for infants (4–6 months); 55 μg Se/day for infants (7–11 months); 70 μg Se/day for children 1–3 years; 95 μg Se/day for children 4–6 years; 130 μg Se/day for children 7–10 years, 180 μg Se/day for children 11–14 years and 230 μg Se/day for adolescents from 15 to 17 years (EFSA NDA Panel, 2023).

3.2.3.1 | *Residue study*

In the tolerance study in chickens for fattening (see Section 3.2.1), data on selenium deposition in tissues and organs (kidney, liver, muscle) of chickens for fattening supplemented with two different sources of selenium at [redacted] were provided.

Results (Table 3) showed that Se deposition significantly increased in all tissues/organs of birds receiving diets supplemented with [redacted] mg Se/kg feed and that deposition of selenium was significantly higher in all tissues in the group receiving Plexomin Se 3000 with respect to the other authorised selenium source.

TABLE 3 Total selenium content in edible tissue of chickens at the end of the trial.

[redacted]

a-c [redacted]

* [redacted]

No data on selenium deposition in skin and fat were provided. The Panel notes that selenium content in body lipids is considered to be low and its contribution to the consumer exposure is considered to be negligible (EFSA FEEDAP Panel, 2011).

In addition, the applicant made reference to several studies and publications, containing information on selenium deposition in animal tissues, that were already assessed by the FEEDAP Panel in its previous opinion (EFSA FEEDAP Panel, 2019a).

[59] Technical dossier/Section III_Safety.

The Panel notes that, in most of these studies, the animals were fed complete feed supplemented with concentrations of organic selenium higher than the one currently authorised (0.2 mg/kg feed), and with the test item different from the one under assessment. Therefore, these studies were not further considered for the assessment.

3.2.3.2 | *Assessment of consumer exposure*

In its opinion form 2011, the FEEDAP Panel estimated the exposure of the consumer to selenium derived from food of animal origin (EFSA FEEDAP Panel, 2011), and concluded that selenium could be considered safe for the consumer when a maximum content of selenium from organic origin of 0.2 mg/kg complete feed would be authorised, within the current authorisation of 0.5 mg total Se/kg complete feed. In its subsequent opinion (EFSA FEEDAP Panel, 2012a, 2012b), the FEEDAP Panel further noted that 'there are likely no principal differences in the metabolic behaviour of selenium from different selenised yeasts (mainly Se-Met) when fed to animals. Selenium deposition from the use of these selenised yeasts as feed additives would therefore result in similar selenium tissue and product concentrations'. Therefore, the conclusion that 0.2 mg organic selenium/kg complete feed should not be exceeded was applied to all organic selenium sources, respecting the maximum total selenium content of 0.5 mg/kg complete feed, to ensure consumer safety (EFSA FEEDAP Panel, 2018a).

The Panel notes that the data from the residue study in chicken provided by the applicant, although limited, might indicate that the selenium deposition in tissues could be source dependent.

Since a new upper tolerable level (UL) (255 µg Se/day for adults), lower than the one available at the time of the previous assessments, was recently proposed (EFSA NDA Panel, 2023), the FEEDAP Panel considers that an updated estimate of the consumer exposure to selenium deriving from the additive is necessary. According to the Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017a, 2017b, 2017c, 2017d), information on residues of selenium from the additive in tissues and products from all animal species (mammals, poultry and fish) is required to perform the estimate of consumer exposure.

The applicant submitted residue data in liver, kidney and muscle of chickens for fattening (see Section 3.2.3.1), but no data on Se deposition in eggs or in tissues and products from other species fed diets supplemented with the additive under assessment at 0.2 mg Se/kg were made available. In the absence of that information, the FEEDAP Panel is not in the position to estimate consumer exposure to selenium from the additive under assessment.

3.2.3.3 | *Conclusions on safety for the consumer*

Due to the lack of complete information on selenium deposition in animal tissues and products, the FEEDAP Panel is not in the position to estimate consumer exposure and to compare it with the updated UL of Se. Therefore, the FEEDAP Panel cannot conclude on the safety of the additive for the consumer.

3.2.4 | Safety for the user

3.2.4.1 | *Effect on respiratory system*

No specific studies were provided by the applicant regarding the toxicity of the additive on the respiratory system.

The highest dusting potential measured for Plexomin® Se 3000 (micro) was [redacted] and the selenium concentration in the dust was up to [redacted] (Section 3.1.4). It can be calculated that a maximum concentration of [redacted] could be released by the dust when handling the additive. A conservative estimate of respirable selenium from dust would be 0.75 mg Se/m^3, assuming that the dust consists only of particles below 50 µm and its respirable fraction (< 10 µm) is about 50%. The threshold limit values (TLVs) for selenium compounds, maximum tolerable air concentrations between 0.02 and 0.2 mg Se/m^3 have been set by different organisations (e.g. Deutsche Forschungsgemeinschaft (DFG) Maximale Arbeitsplatz Konzentration (MAK) List, Occupational Safety and Health Administration (OSHA)-Permissible Exposure Limit (PEL), and National European Authorities). Considering that the above estimate of respirable selenium from the dust of the additive, in its micro form, exceeds the occupational threshold limits, its handling presents a risk by inhalation.

The exposure through inhalation is unlikely for Plexomin® Se 3000 (granules) since it is dust-free. Due to the proteinaceous nature, the additive (both forms) is considered a respiratory sensitiser.

3.2.4.2 | *Effect on eyes and skin*

No studies on skin and eye irritation have been provided for Plexomin® Se 3000 (granules).

The skin irritation potential of Plexomin® Se 3000 (micro) was tested in a study performed according to OECD Testing Guideline 439.[60] The test demonstrated that the additive (micro form) is not a skin irritant.

The eye irritation potential of Plexomin® Se 3000 (micro) was tested in a study performed according to OECD TG 492.[61] The test demonstrated that the additive (micro form) is not an eye irritant.

No data regarding the skin sensitisation potential of the additive were available. The FEEDAP Panel notes that the OECD test guidelines available at present are designed to assess the skin sensitisation potential of chemical substances only and

[60]Technical dossier/Section III/Annex III.92.

[61]Technical dossier/Section III/Annex III.95.

that currently, no validated assays for assessing the sensitisation potential of inactivated microorganisms are available. Therefore, no conclusion can be drawn on the skin sensitisation potential of the additive (both forms).

3.2.4.3 | *Conclusions on safety for the user*

Plexomin® Se 3000 (granules) is dust-free; therefore, the exposure through inhalation is unlikely. Plexomin® Se 3000 (micro) represents a risk by inhalation. Both forms of the additive (granules and micro) are regarded as respiratory sensitisers, due to their proteinaceous nature.

Plexomin® Se 3000 (micro) is not irritant to the skin and the eyes. Due to the lack of data, no conclusions can be drawn on the dermal and eye irritation potential of Plexomin® Se 3000 (granules). No conclusion can be drawn on dermal sensitisation potential for any of the forms.

3.2.5 | Safety for the environment

To assess the environmental risk of selenium from the additive, the Panel compared the worst-case predicted environmental concentrations (PECs),[62] calculated at the maximum authorised level of selenium, with the natural background concentration considered as 90th percentile value from FOREGS Geochemical Baseline Database.[63] If the predicted concentrations fall below 10% of this value, no further risk assessment is needed for trace elements. The determination of natural background concentration for trace elements in water is described in the Guidance for implementing environmental quality standards (EQSs) for metals, as outlined in the Water Framework Directive implementation strategy.[64]

The 90th percentile of selenium in (surface) freshwater from 807 water samples collected throughout Europe for the FOREGS survey was 1.1 µg Se/L.

The FOREGS database does not contain data on selenium in soil or marine sediment, therefore, to cover the data gap for these two compartments, the applicant conducted a literature search.[65]

The literature search [redacted][66]

The FEEDAP Panel notes that literature data on exact values of selenium in European soils are scarce; however, the few studies from the literature review, providing detailed values, were assessed and used for setting the background selenium level in soils to be used in the present evaluation. Limited background data are available on selenium in marine sediment in Europe.

3.2.5.1 | *Environmental safety from use in feeds for terrestrial farm animals*

The worst-case PEC_{soil} calculated at a use level of 0.2 mg/kg feed is 4.03 µg Se/kg dry weight (dw) soil, for pigs for fattening. [redacted] Since the mean of Se in soil is two orders of magnitude higher than the calculated PEC_{soil}, no further risk assessment is needed.

3.2.5.2 | *Environmental safety from use in aquaculture feeds*

The worst-case PEC_{swaq} in land-based aquaculture was 0.001 µg/L for salmonids. This PEC_{swaq} is two orders of magnitude below the background level (10% of the 90th percentile is 0.11 µg Se/L). The risk to surface water is not expected when using selenium in aquaculture feed on land-based fish farms.

No data were available on the selenium background levels in marine sediment in Europe. Nevertheless, information gathered from the literature search performed by the applicant indicates that selenium does not accumulate in marine sediments, but tends to be mobilised in the water column (Meseck & Cutter, 2012). Bacterial and/or plankton species can form various volatile selenium species by methylation, contributing to the release of selenium from estuaries and marine sediment. Therefore, no risk for the marine sediment compartment is expected when the additive is used according to the proposed use levels.

[62]Feed additives environmental risk assessment (FERA) tool available online: https://www.efsa.europa.eu/en/applications/feedadditives/tools

[63]Data available in FORGES database. Geochemical Atlas of Europe; copyright © 2005 the Association of the Geological Surveys of The European Union (EuroGeoSurveys)/ the Geological Survey of Finland. Available online: http://weppi.gtk.fi/publ/foregsatlas/ForegsData.php

[64]Guidance document N38. Technical Guidance for implementing Environmental Quality Standards (EQS) for metals. Consideration of metal bioavailability and natural background concentrations in assessing compliance (2019). Common Implementation Strategy for the Water Framework Directive (2000/60/EC). Available online: https://metals-toolbox.com/uploads/pdf/environment/Guidance%2520No%252038%2520-%2520Technical%2520guidance%2520for%2520EQS%2520for%2520metals%2520(2).pdf

[65]Technical dossier/Supplementary information 2023-09-15.

[66]Technical dossier/Supplementary information 2023-09-15/Annex_SIn_III_3.

3.2.5.3 | *Conclusions on the safety for the environment*

The FEEDAP Panel concludes that the use of the additive in animal nutrition at the proposed conditions of use is considered safe for the environment.

3.3 | Efficacy

The applicant submitted a tolerance/efficacy trial to demonstrate that the additive is efficacious in supplying Se to the animal. The trial is described above in Section 3.2.2. The supplementation of feed for chickens for fattening with the additive under evaluation and an alternative source of selenium ([redacted]) at a level of [redacted] mg Se/kg feed for 37 days showed significantly higher concentrations of selenium and [redacted] in [redacted] compared to the control, while no differences were observed in comparison with the reference source of selenium [redacted] (Table 4).

TABLE 4 Selenium (μg Se/L) and [redacted]

Selenium source	Selenium added (mg/kg complete feed)	Selenium (μg/L)	[redacted]
None	–	[redacted]	[redacted]
Plexomin® Se 3000	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[a,b]Values in a column without a common superscript are significantly different ($p \leq 0.05$).

As shown above, the use of Plexomin® Se 3000 resulted in higher selenium deposition in liver, kidney and muscle compared to both the reference selenium source and the control group (Table 3).

The FEEDAP Panel concludes that Plexomin® Se 3000 is an effective source of selenium for chickens for fattening. The conclusion can be extrapolated to all animal species.

3.4 | Post-market monitoring

The FEEDAP Panel considers that there is no need for specific requirements for a post-market monitoring plan other than those established in the Feed Hygiene Regulation[67] and good manufacturing practice.

4 | CONCLUSIONS

Saccharomyces cerevisiae CCTCC M 2022402 is considered by EFSA as suitable for the QPS approach to safety assessment and consequently it raises no safety concerns.

The additive under assessment is considered safe for all animal species provided that the maximum authorised selenium content in complete feed (0.2 mg Se/kg feed from organic source, 0.5 mg total Se/kg feed) is not exceeded.

In the absence of complete data on selenium deposition in animal tissues and products, the FEEDAP Panel is not in the position to conclude on the safety of the additive for the consumer.

Plexomin® Se 3000 (granules) is dust-free; therefore, the exposure through inhalation is unlikely. Plexomin® Se 3000 (micro) presents a risk by inhalation. Both forms of the additive (granules and micro) are considered as respiratory sensitisers. Plexomin® Se 3000 (micro) is not irritant to the skin and the eyes. Due to the lack of data, no conclusions can be drawn on the dermal and eyes irritation potential of the Plexomin® Se 3000 (granules). No conclusions can be drawn on the dermal sensitisation potential of both forms of additive.

The use of the additive is considered safe for the environment, when used under proposed conditions of use.

The additive is an efficacious source of selenium in feedingstuffs for all animal species.

ABBREVIATIONS

ADME absorption, distribution, metabolism, and excretion
ANS EFSA Scientific Panel on Additives and Nutrient Sources added to Food
BW body weight
CD Commission Decision
CEF EFSA Scientific Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
CFU colony forming unit

[67]Regulation (EC) No 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

CV coefficient of variation
EURL European Union Reference Laboratory
FAO Food Agricultural Organization
FEEDAP EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
LOD limit of detection
LOQ limit of quantification
MCHC mean corpuscular haemoglobin concentration
MCV mean corpuscular volume
OECD Organisation for Economic Co-operation and Development
RH relative humidity
SCF Scientific Committee on Food

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CONFLICT OF INTEREST
If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

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NOTE
Safety and efficacy of a feed additive consisting of inactivated selenised yeast (*Saccharomyces cerevisiae* CCTCC M 2022402) for all animal species was adopted by EFSA's Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) on the 31st January 2024. After this date, the data used to establish the safety of the additive for the environment had to be revised and the text has been modified accordingly. The FEEDAP Panel re-adopted the opinion with the modified text on the 12 March 2024. The modified text had no impact on the conclusion.

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